8.3
The S_N2 Mechanism of Nucleophilic Substitution

Kinetics

Many nucleophilic substitutions follow a second-order rate law.

$CH_3Br + HO^- \varnothing CH_3OH + Br^-$

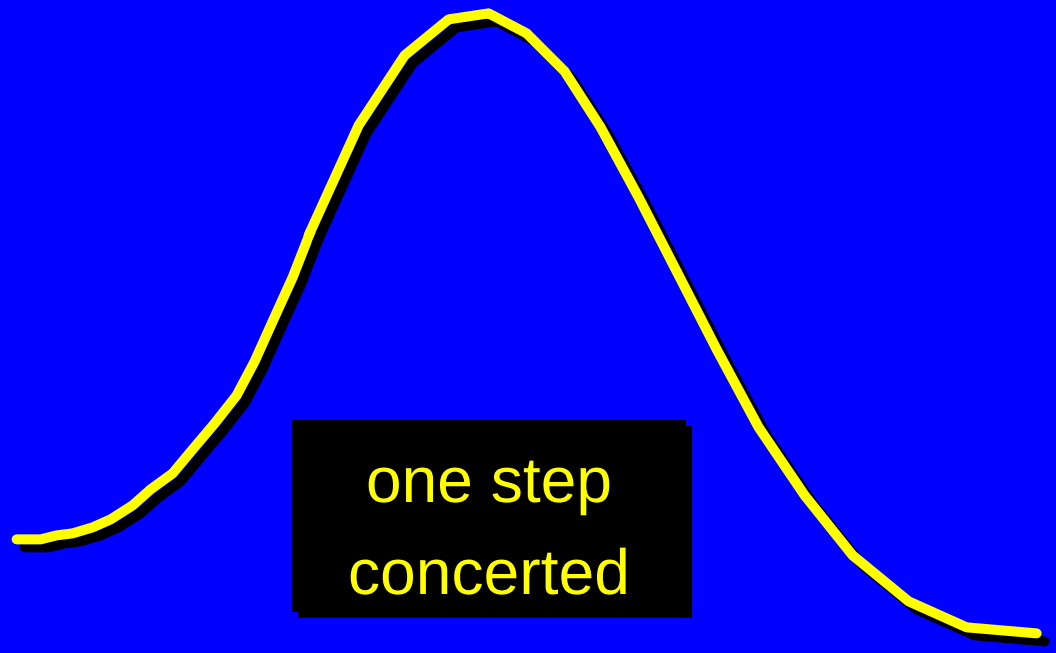
rate = $k[CH_3Br][HO^-]$

inference: rate-determining step is bimolecular

Bimolecular mechanism

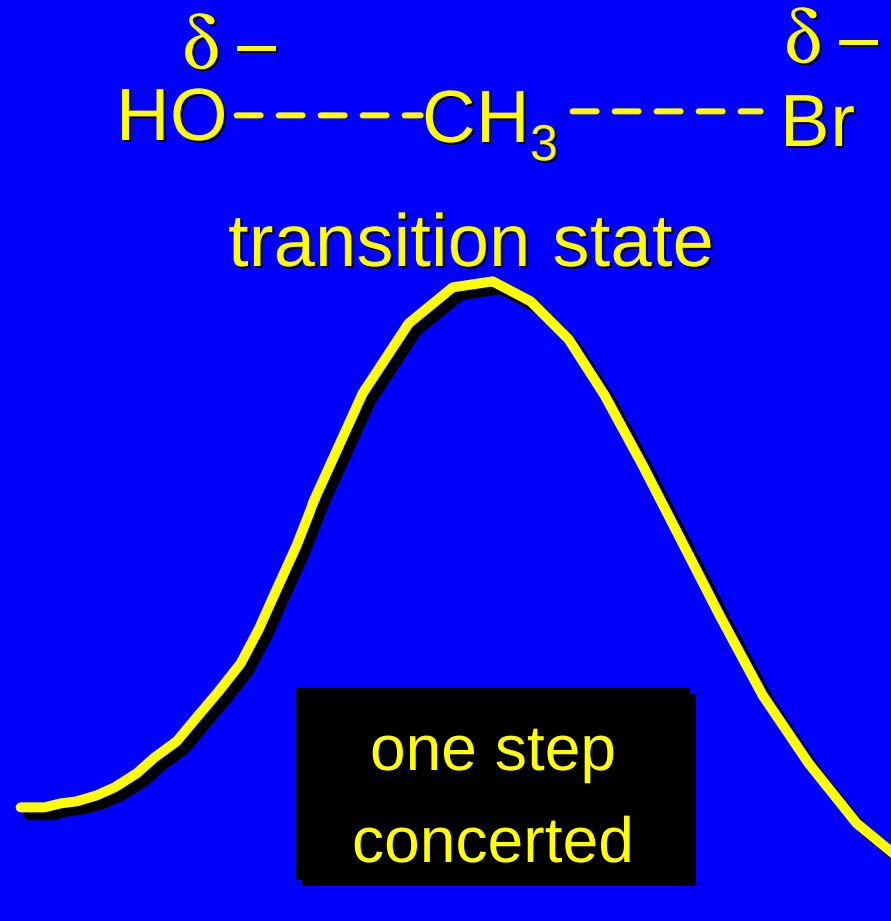
one step
concerted

Bimolecular mechanism



$$HO^- + CH_3Br \longrightarrow HOCH_3 + Br^-$$

Bimolecular mechanism



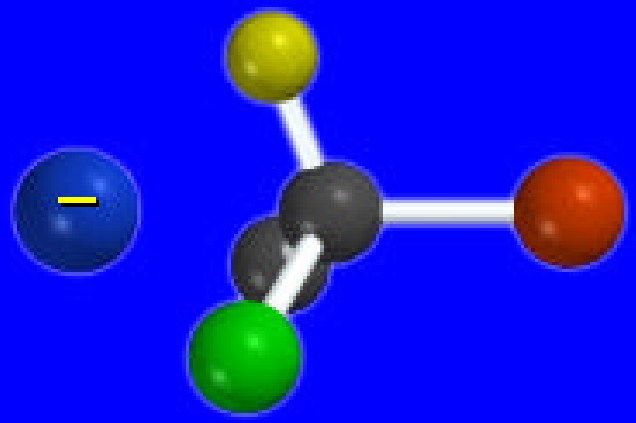
$$HO^- + CH_3Br \longrightarrow HOCH_3 + Br^-$$

8.4
Stereochemistry of S_N2 Reactions

Generalization

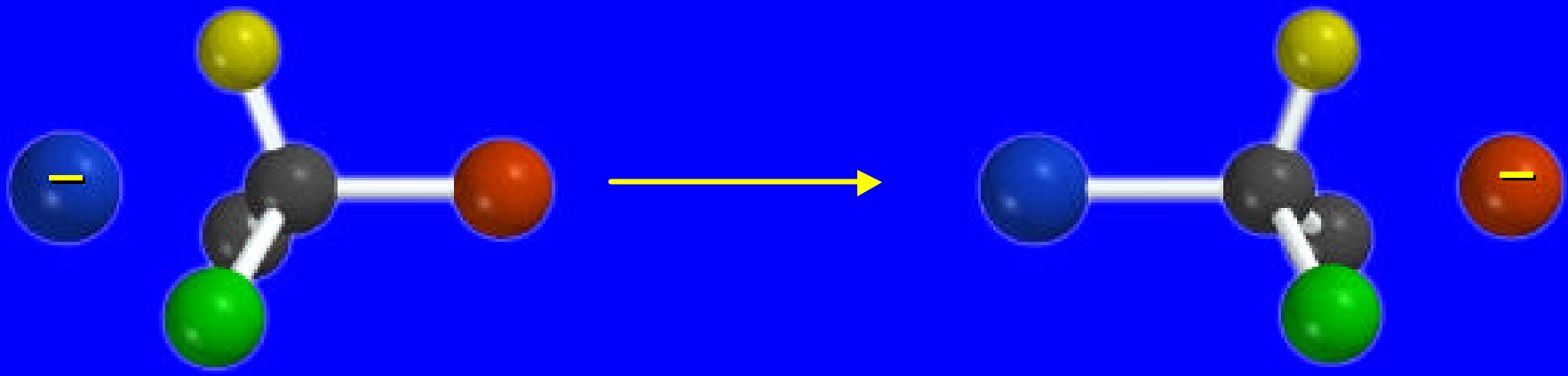
Nucleophilic substitutions that exhibit second-order kinetic behavior are stereospecific and proceed with inversion of configuration.

Inversion of Configuration



nucleophile attacks carbon
from side opposite bond
to the leaving group

Inversion of Configuration



nucleophile attacks carbon from side opposite bond to the leaving group

three-dimensional arrangement of bonds in product is opposite to that of reactant

Stereospecific Reaction

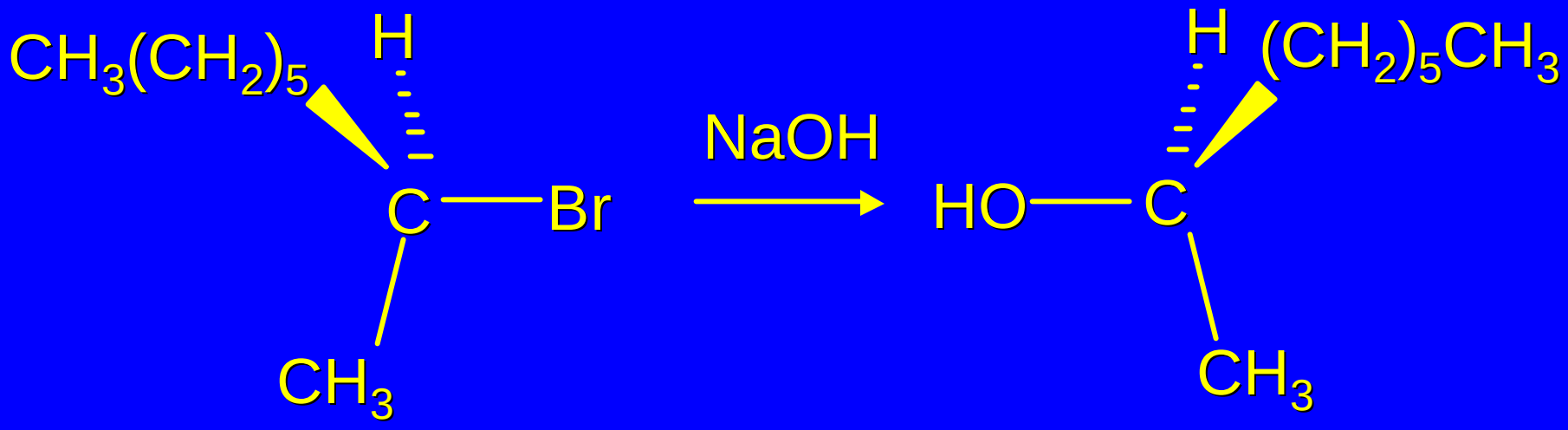
A stereospecific reaction is one in which stereoisomeric starting materials give stereoisomeric products.

The reaction of 2-bromooctane with NaOH (in ethanol-water) is stereospecific.

(+)-2-Bromooctane ∅ (–)-2-Octanol

(–)-2-Bromooctane ∅ (+)-2-Octanol

Stereospecific Reaction



(*S*)-(+)-2-Bromooctane

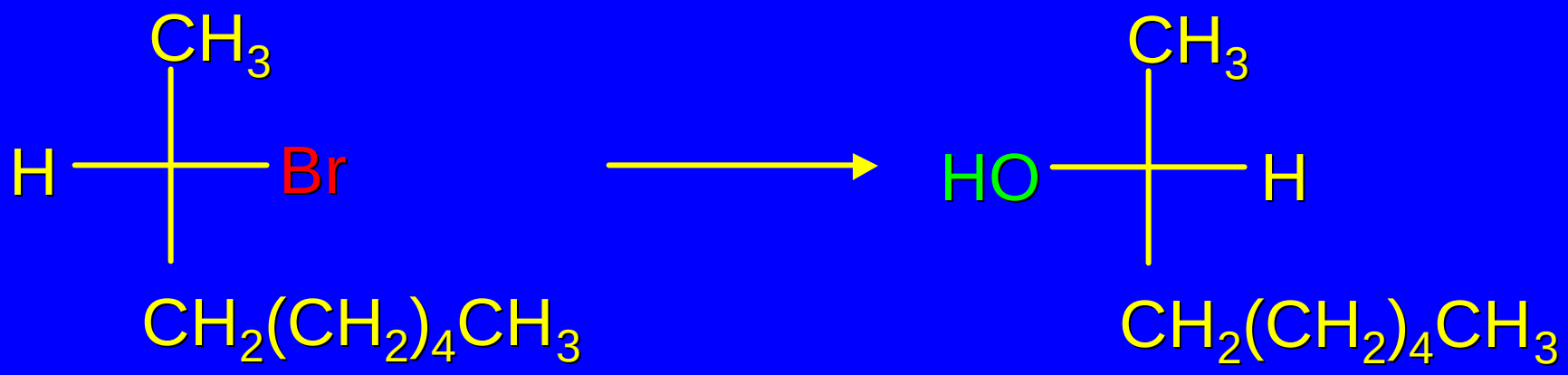
(*R*)-(–)-2-Octanol

Problem 8.4

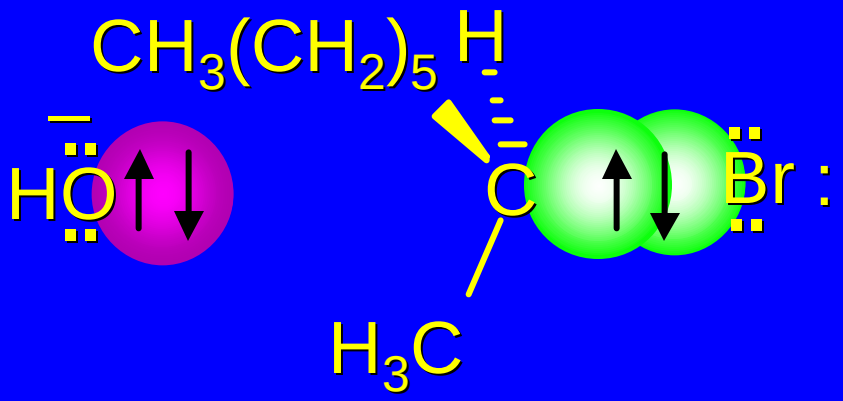
The Fischer projection formula for (+)-2-bromooctane is shown. Write the Fischer projection of the (–)-2-octanol formed from it by nucleophilic substitution with inversion of configuration.

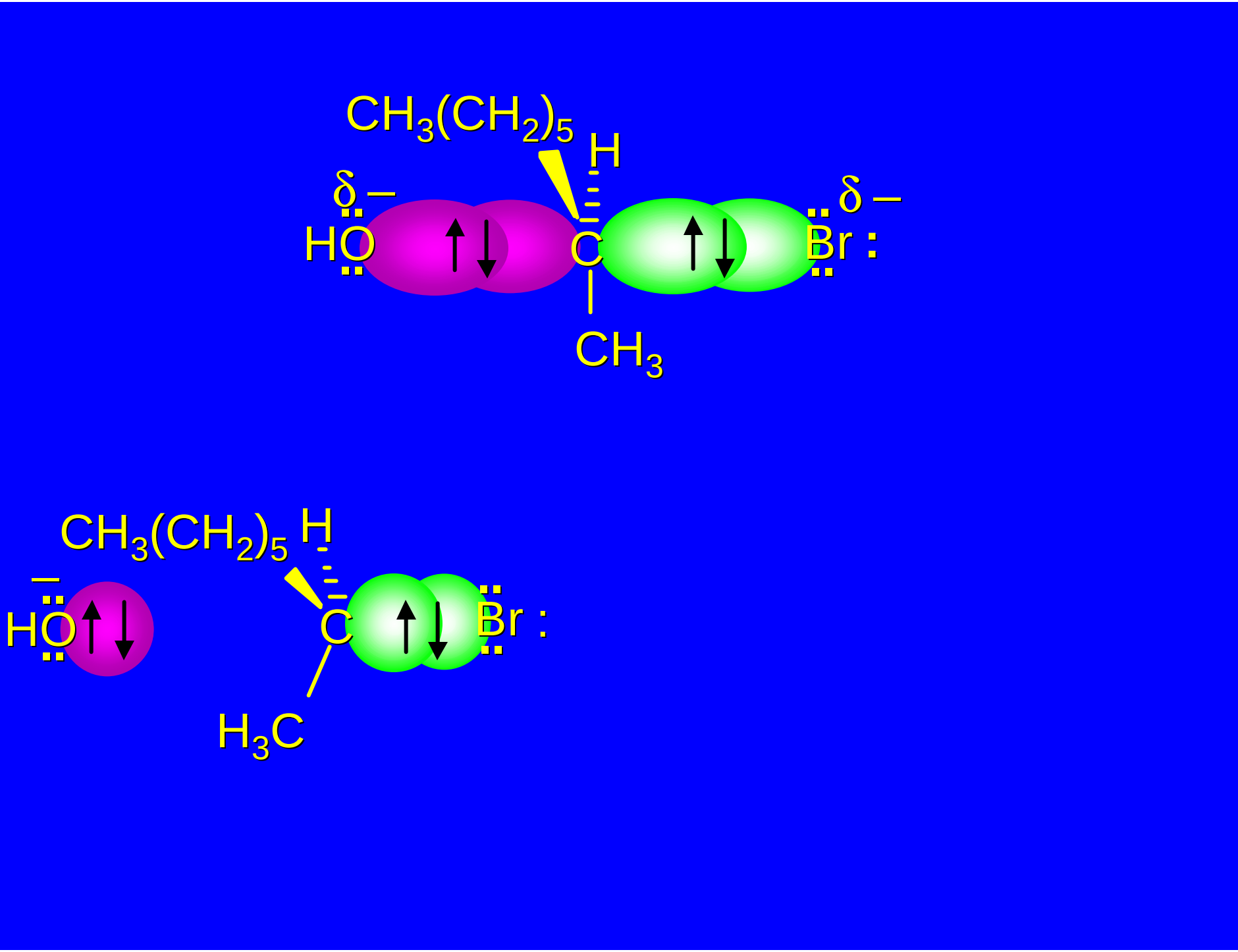
Problem 8.4

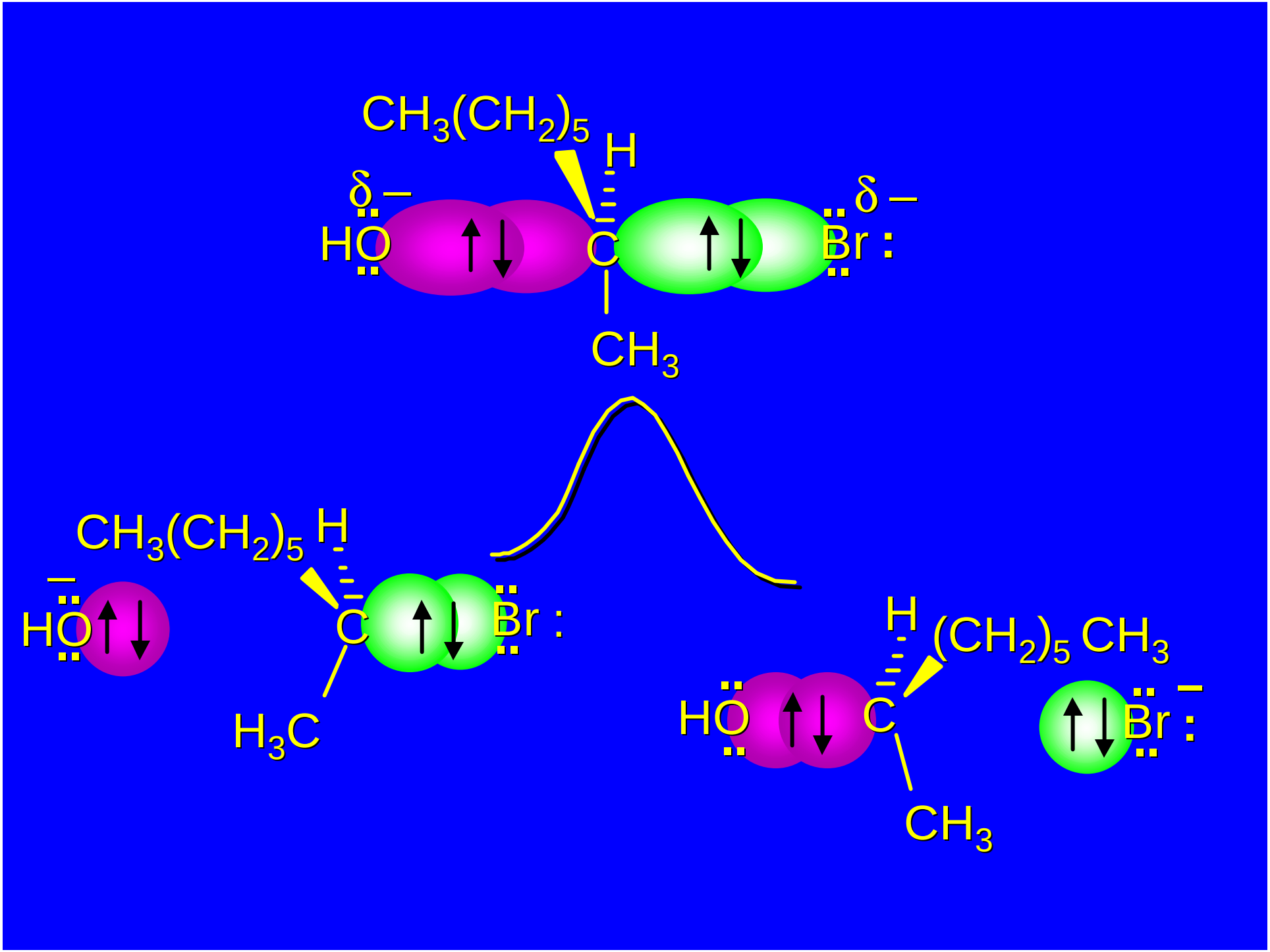
The Fischer projection formula for (+)-2-bromooctane is shown. Write the Fischer projection of the (–)-2-octanol formed from it by nucleophilic substitution with inversion of configuration.



8.5
How S_N2 Reactions Occur


CH3(CH2)5
H
HO
C
Br :
H3C


CH3(CH2)5
H
δ –
HO
C
Br :
δ –
CH3
CH3(CH2)5
H
HO
C
Br :
H3C


CH3(CH2)5
H
δ –
HO
C
Br :
δ –
CH3
CH3(CH2)5
H
HO
C
Br :
H3C
H
(CH2)5 CH3
HO
C
Br :
CH3

8.6
Steric Effects in S_N2 Reactions

Crowding at the Reaction Site

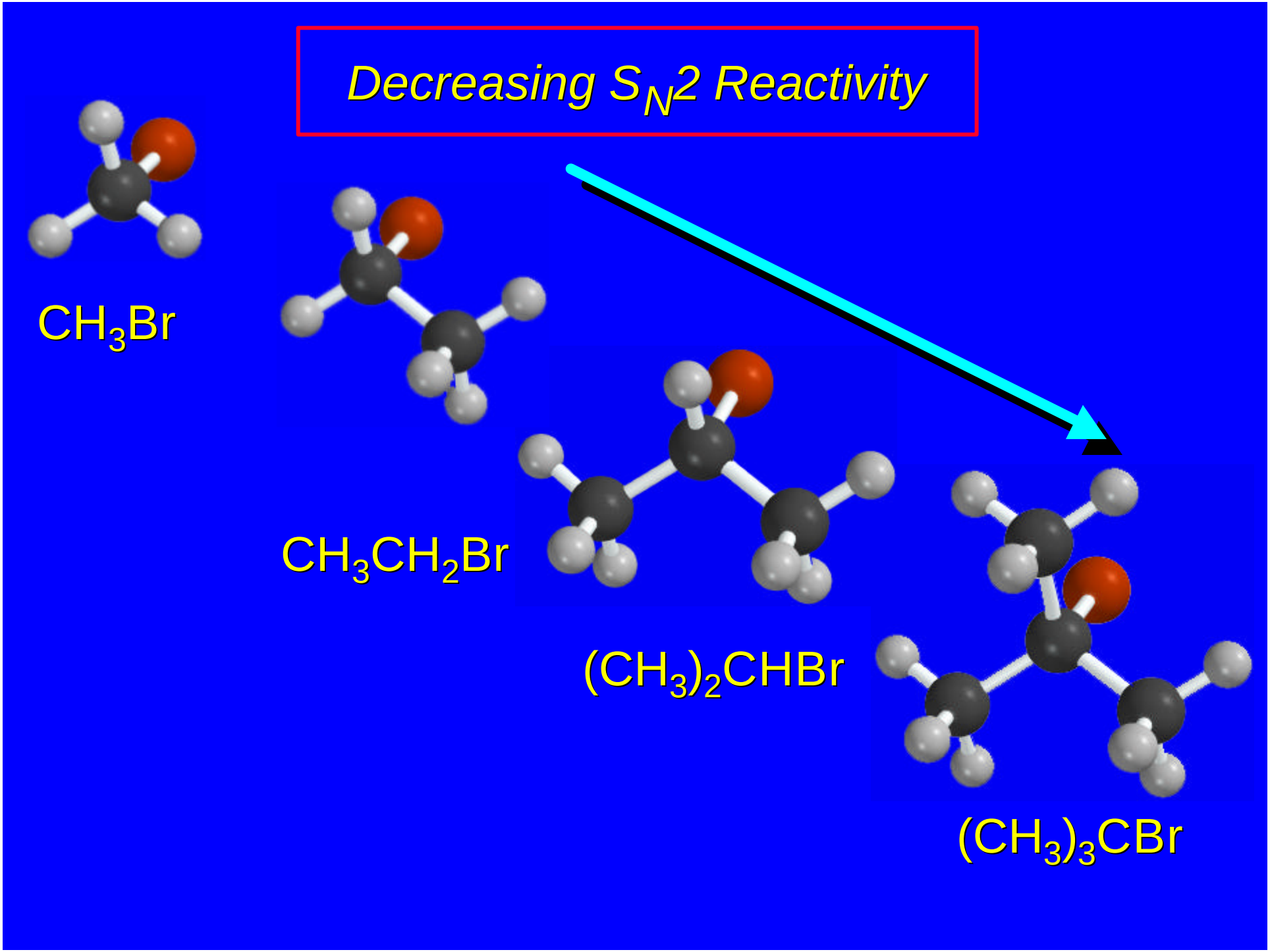
The rate of nucleophilic substitution by the S_N2 mechanism is governed by steric effects.

Crowding at the carbon that bears the leaving group slows the rate of bimolecular nucleophilic substitution.

Table 8.2 Reactivity toward substitution by the S_N2 mechanism

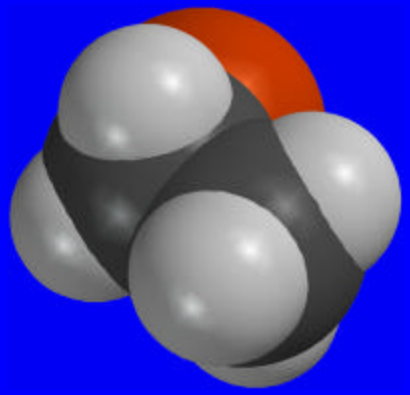
$$RBr + LiI \varnothing RI + LiBr$$

Alkyl bromide	Class	Relative rate
CH_3Br	Methyl	221,000
CH_3CH_2Br	Primary	1,350
$(CH_3)_2CHBr$	Secondary	1
$(CH_3)_3CBr$	Tertiary	too small to measure

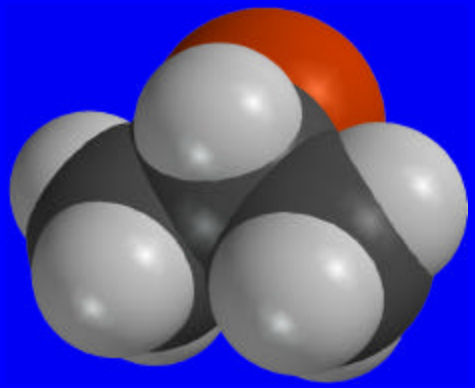

Decreasing S_N2 Reactivity
CH_3Br
CH_3CH_2Br
$(CH_3)_2CHBr$
$(CH_3)_3CBr$

Decreasing S_N2 Reactivity

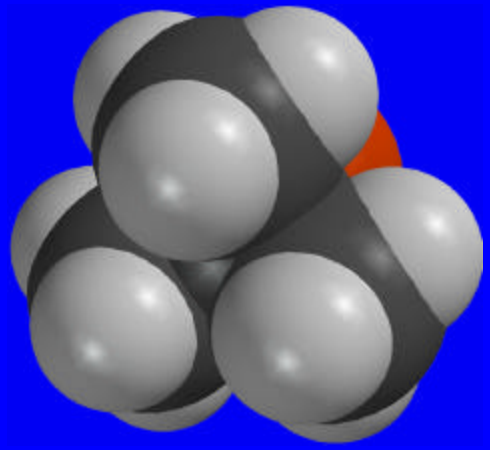
CH_3Br



CH_3CH_2Br



$(CH_3)_2CHBr$



$(CH_3)_3CBr$

Crowding Adjacent to the Reaction Site

The rate of nucleophilic substitution by the S_N2 mechanism is governed by steric effects.

Crowding at the carbon adjacent to the one that bears the leaving group also slows the rate of bimolecular nucleophilic substitution, but the effect is smaller.

Table 8.3 Effect of chain branching on rate of S_N2 substitution

$$RBr + LiI \varnothing RI + LiBr$$

Alkyl bromide	Structure	Relative rate
Ethyl	CH_3CH_2Br	1.0
Propyl	$CH_3CH_2CH_2Br$	0.8
Isobutyl	$(CH_3)_2CHCH_2Br$	0.036
Neopentyl	$(CH_3)_3CCH_2Br$	0.00002